

BOOK OF ABSTRACTS



SYNTHESIS AND CHARACTERIZATION OF NOVEL HYDROXY-AND AMINOBISPHOSPHONATES

<u>Fátima C. Teixeira</u>[§], Carla Lucas[§], Inês F. Antunes[§], M. João M. Curto[§], M. Neves[†] and M. Teresa Duarte[±]

[§] INETI-DTIQ, Estrada do Paço do Lumiar, 22, 1649-038 Lisboa, Portugal
[†] Instituto Tecnológico e Nuclear, Estrada Nacional 10, 2686-953 Sacavém, Portugal
[±] Centro de Química Estrutural, IST, Av. Rovisco Pais, 1, 1049-001 Lisboa, Portugal
E-mail: fatima.teixeira@ineti.pt

Bisphosphonates (BPs) are a family of drugs that are successfully used in the treatment of various calcium-related disorders such as Paget's disease, osteoporosis and bone metastases. In addition, functional BPs have been also used in the treatment of metal intoxication and as novel ligands for well-defined radioactive metal complexes that can be used in imagiology, scintigraphy and radiotherapy applications [1,2].

The indazole derivatives are pharmacologically important compounds and the indazole ring system forms the basis of a number of drug molecules. Condensed pyrazoles are also known as pharmacophoric elements in numerous active compounds. However, in comparison with other heteroaromatic compounds, the chemistry of indazole and condensed pyrazoles remains less studied [3].

The present work is to extend the previous studies in indazolebisphosphonates [4] in order to obtain new BPs derived from indazole and condensed pyrazole with potential biological/therapeutical activities. Herein, we report the synthesis and characterization of a series of new 1-hydroxybisphosphonates (1) and aminobisphosphonates (2) (substituted at different C- or N-positions of the indazole ring - N-1, C-5, C-6, C-7) (Figure 1). Crystal structure of an aminobisphosphonate was determined by X-ray crystallography.



hydroxybisphosphonate 1

aminobisphosphonate 2

Figure 1

[1] H. Fleich, Endocrine Reviews, 1998, 19, 80-100.

[2] W.A. Volkert and T.J. Hoffman, Chem. Rev., 1999, 99, 2269-2292.

[3] F.C. Teixeira, H. Ramos, I.F. Antunes, M.J.M. Curto, M.T. Duarte and I. Bento, *Molecules*, 2006, 11, 867-889.

[4] F.C. Teixeira, I.F. Antunes, M.J.M. Curto, M. Neves and L. Gano, *Medicinal Chemistry in the 21st Century*, 2006, P89; F.C. Teixeira, I.F. Antunes, M.J.M. Curto, R. Fausto, M. Rosado and M. Neves, *Medicinal Chemistry in the 21st Century*, 2006, P90.

Acknowledgments: To FCT (FEDER, POCI) for provision of funding (POCI/QUI/55508/2004).